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毛喉鞘蕊花的微量成分*

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摘要　从唇形科毛喉鞘蕊花（*Coleus forskohlii*）全草的氯仿提取物分离到2个新的微量成分，鞘蕊花戊素和已素。基于光谱分析，鞘蕊花戊素和已素的化学结构分别鉴定为1α,7β－二乙酰氧基－8,13－环氧－6β羟基勒丹－14烯－11－酮(1)和7β－乙酰氧基－8,13环氧－6β,9α－二羟基勒丹－14烯－11－酮(2)。

关键词　鞘蕊花戊素，鞘蕊花已素，毛喉鞘蕊花，唇形科，二维核磁共振谱
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Minor Constituents from *Coleus forskohlii*

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Abstract　Two new labdanoids, forskolin E and F, with forskolin A, B, C and D, have been isolated from the chloroform extract of the whole plants of *Coleus forskohlii*. The chemical structures of the two minor constituents have been established as 1α,7β－diacetoxy－8,13 epoxy－6β－hydroxylabd－14－en－11－one(1) and 7β－acetoxy－8,13－epoxy－6β,9α－dihydroxylabd－14－en－11－one(2), respectively, on the basis of detailed spectroscopic analysis and all assignments were supported by $^{1}H-^{1}H$ COSY, HMBC and HMQC spectrum (see table 1).

Key words　Forskolin E and F, *Coleus forskohlii*, Labiatae, 2DNMR

Coleus forskohlii is distributed only in northeast region of Yunnan in China. The decoction of the plant are used in local folk medicine against asthma, congh and bronchitis. In previous paper (Jin *et al*, 1990) we reported four constituents, forskolin A, B, C and D, isolated form *Coleus forskohlii*. Meanwhile we excavated the plant into a new drug of national degree for the treatment of asthma, cough, bronchitis and acute coming on chronic bronchitis in seven years ago. The present parper was dscribed the isolation and the structural determination of minor constituents, forskolin E and F, from same plant source.

The pharmacological test of minor constituents showed that compared with previous four constituents, it's activity is a marked decrease, because there is no hydroxy group at 1 or 9 position. Sea-

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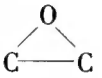
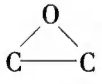
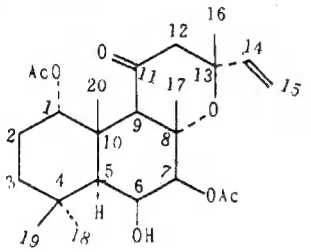
mon *et al* (1983) reported, the 1 and 9 hydroxy groups of forskolin are important for biological activity. Thus, the 1, 9 dideoxy derivative of forskolin does not stimulate adenylate cyclase. Two point of contact critical to the drug – receptor inter – action have been identified which are the 1α – and 9α – OH groups. So it is mainly the 1,9 – locus and the olefinic locus that is proposed in this interface to have a bearing on the order of potency and profile of forskolin (Harms, 1986).

RESULTS AND DISCUSSION

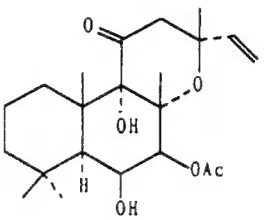
Forskolin E(1), $C_{24}H_{36}O_7$, $[M]^+$ 436, showed the presence of five tertiay methyl groups, four methylene groups, six methine group, four quaternary carbons, one olefinic carbon, one ketonic carbon and two acetoxy signals in ^{13}C NMR(DEPT) spectrum (Table 2). It is labdanolic diterpene. Judging from the following spectral data: no UV adsorption; IRν_{max}^{KBr} cm^{-1}: 3400(OH), 1700(C=O), 1640(C=C), 1730, 1256();^1H NMR δ: 2.70, 2.83 (each H, d, J=18.2Hz, 12 – H);^{13}C NMR δ: 146.5(d), 112.9 (t) (double bond), 206.3(s) (ketone)(Jin *et al*, 1990). Its IR spectrum showed the characteristic absorption of hydroxy groups at 3509, ester groups at 1738, 1230, double bond at 1640 and epoxy at 1370, 1256. The presence of two secondary acetoxy groups was suggested by its ^1H NMR data; δ 2.04, 2.11(6H, s, 2×OAc) and two proton signals at 4.77 (1H, t, J=2.6 Hz, H – β), 5.59(1H, d, J=4.0Hz, H – 7α) attached to the acetoxy – bearing carbon, one hydroxy signal at 6.80 (1H, OH). By comparision of ^{13}C NMR data of previous compunds, caused the upfield shift of the signal for C_9(δ 80.4) to 58.4. Compound (1) was acetylated under ordinary condition, tricetyl – compound was not obtained, revealing that hydroxy group at C – 6 was sterically hindered, meanwhile indicated that two acetoxy groups must be located at C_1 and C_7 position. The above – mentioned data suggested this compound has a typical 11 – oxo – 8, 13 – epoxy – 14 – en – 11 – one labdane nucleus as a basis skeleton (Bhat *et al*, 1977). Therefore, the chemical sturcure of forskolin E(1) could be represented as 1α,7β – diacetoxy – 8, 13 – epoxy – 6β – hydroxylabd – 14 – en – 11 – one.

Forskolin F(2), $C_{22}H_{34}O_6$, $[M]^+$ 394, showed the presence of five tertiary – methyl groups, five methylene groups, four methine groups, five quaternary carbons one olefinic carbon, one ketonic carbon and one acetoxy signal in ^{13}C NMR(DEPT) spectrum (Table 2). Judging from the following spectral data: no UV absorptium; IRν_{max}^{KBr} cm^{-1}: 3450(OH), 1705(C=O), 1642(C=C), 1370, 1258 ();^1H NMR δ: 2.76, 2.83(each H, dd, J=18.2, H – 12);^{13}C NMR δ: 147.0(d), 111.8(t)(double bond), 207.1(s) (ketone)(Jin *et al*, 1990). Its IR spectrum showed the characteristic absorption of hydroxy groups at 3500, ester groups at 1732, 1231, double bond at 1641 and epoxy at 1371, 1254. The presence of one acetoxy group was suggested by its ^1H NMR data: δ 2.12(3H, s, OAc) and one proton at 5.59(1H, d, J=4.0Hz, H – 7α) attached to the acetoxy – bearing carbon, two secondary hydroxy signal at δ 5.28(1H, br. s). By comparision of the ^{13}C NMR of previous compounds, caused the upfield shift of the signal for C_1(δ70.3) to δ36.4.

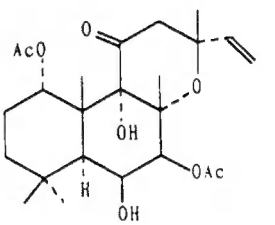
Compound (2) was acetylated under ordinary condition, diacetyl – compound was not obtained, revealing that hydroxy group at C – 6 was sterically hindered, meanwhile indicated that the acetoxy group must be located at C_7 position. The above – mentioned data suggested this compound has a typical 11 – oxo – 8, 13 – epoxy – 14 – en – 11 – one labdane nucleus as a basis skeleton (Bhat *et al*, 1977). Therefore, the chemical structure of forskolin F(2) could be represented as 7β – acetoxy – 8, 13 – epoxy – 6β,9α dihydroxylabd – 14 – en – 11 – one.



forskolin E (1)



forskolin F (2)



forskolin B (3)

Table 1　Correlation of ^1H NMR and HMBC of forskolin E and F(in C_5D_5N)

HMBC observed	^1H NMR assignment	HMBC observed	^1H NMR assignment
E　C – 1	1 – H,2 – H,20 – H	F　C – 1	1 – H, 2 – H, 20 – H
C – 2	2 – H,3 – H	C – 2	2 – H,3 – H
C – 3	2 – H, 3 – H	C – 3	3 – H, 2 – H, 19 – H
C – 4	2 – H, 18 – H, 19 – H	C – 4	5 – H, 18 – H, 19 – H
C – 5	5 – H, 9 – H, 20 – H	C – 5	5 – H, 18 – H
C – 6	6 – H, 7 – H	C – 6	6 – H, 7 – H
C – 7	6 – H, 7 – H	C – 7	6 – H, 7 – H
C – 8	6 – H, 7 – H, 9 – H	C – 8	6 – H, 7 – H
C – 9	6 – H, 17 – H, 20 – H	C – 9	7 – H, 20 – H
C – 10	9 – H, 20 – H	C – 10	1 – H, 20 – H
C – 11	9 – H, 12 – H	C – 11	12 – H
C – 12	12 – H, 16 – H	C – 12	12 – H, 16 – H
C – 13	12 – H, 14 – H, 16 – H	C – 13	12 – H, 14 – H, 16 – H
C – 14	12 – H, 15a – H, 16 – H	C – 14	12 – H, 15a – H, 16 – H
C – 15	15a – H, 15b – H	C – 15	15a – H, 15b – H

Table 2 ^{13}C NMR data of forskolin E(1), F(2), B(3) in C_5D_5N

Carbon	1	2	3	Carbon	1	2	3
1	70.3d	36.4t	71.5d	13	75.5s	76.1s	75.8s
2	26.0t	27.1t	27.2t	14	146.5d	147.0d	147.4d
3	36.9t	36.2t	36.5t	15	112.9t	111.8t	110.9t
4	34.2s	35.4s	35.2s	16	31.7q	31.4q	30.8q
5	46.3d	46.2d	46.4d	17	24.3q	25.1q	26.0q
6	70.3d	70.8d	71.0d	18	32.9q	33.0q	32.8q
7	79.6d	80.1d	80.0d	19	23.3q	23.5q	24.1q
8	78.8s	78.5s	78.6s	20	18.1q	18.5q	18.7q
9	58.4d	80.2s	80.4s	O=C	170.4s	169.5s	169.5s
10	42.6s	42.5s	41.5s		170.4s		170.2s
11	206.3s	207.1s	206.9s	CH_3	21.2q	21.5q	21.5q
12	50.2t	50.1t	49.5t		21.9q		21.8q

EXPERIMENTAL SECTION

General kofler melting points were uncorrected; optical rotations were taken on a Jasco – 20C digital polarimeter. IR were recorded on KBr discs with a Bio – Rad FTS – 135 spectrometer. EIMS (positive) were measured on a VG Auto spec – 3000 spectrometer with direct inlet 70 or 20eV. NMR were run on a Brucker AM – 500 spectrometer using TMS as internal standard. Chemical shift values are reported in δ(ppm) units (C_5D_5N). Coupling constants (J) were expresent in Hz.

Plant material The same plant material was used as in previous report (Jin *et al*, 1990).

Extraction and isolation of constituents The residue (5.0g) from previous report was further submitted to CC (silie gel), eluting with acetone – petroleum (bp. 60 ~ 90℃) and increasing proportions of acetone. Fractions were monitored by TLC. All components were further purified by prep TLC (silica gel) and recrystallization yielding in order of increasing polartites: forskolin E(1, 16.0mg) and forskolin F(2, 20.0mg). The physical properties of the isolated compound were as follow:

Forskolin E(1): $C_{24}H_{36}O_7$, M 436, colorless needles, mp 156 ~ 158 ℃; $[\alpha]_D^{26}$ – 26.25(c 0.42, MeOH), IRν_{max}^{KBr} cm^{-1}: 3509, 1738, 1723, 1707, 1642, 1370, 1258, 1175, 1021 951; EIMS m/z: 436[M^+], 418(35), 390(45), 376(60), 316(56), 43(100): ^1H NMR (500MHz, C_5D_5N): δ: 0.94, 0.98, 1.24, 1.66, 1.78(each 3H,s,5 × Me), 2.04, 2.11(each 3H, s, 2 × OAc), 4.77 (1H,t. J=2.6Hz, H – 1β), 1.66(1H, dtd, J=13.2, 3.6, 2.6Hz, H – 2α), 2.13 (1H, tdd. J=13.2, 3.6Hz, H – 2β), 2.01(1H, *td*, J=13.2, 3.6Hz, H – 3α), 1.05(1H, td, J=13.2, 3.6, H – 3β), 2.07(1H, d J=2.2Hz, H – 5α), 6.14(1H, dd, J=4.0, 2.2Hz, H – 6α), 5.59(1H,d,

J=4.0Hz, H-7α), 4.17(1H, s, H-9α), 2.76(1H, d, J=18.2Hz, H-12α), 2.83(1H, d, J=18.2Hz, H-12β), 5.99(1H, dd, J=17.4, 10.8Hz, H-14), 4.40(1H, dd, J=5.4, 0.8Hz, H-15a), 4.99(1H, dd, J=10.8, 0.8Hz, H-15b). ^{13}C NMR(500MHz, C_5D_5N) δ: see Table 2.

Forskolin E(2), $C_{22}H_{34}O_6$, M 394, colorless needles, mp 165~167℃; $[\alpha]_D^{26}$ -35.27° (c 0.45, MeOH). IRν_{max}^{KBr} cm^{-1}: 3500, 1732, 1705, 1640, 1370, 1256, 1170, 1021, 950; EI m/z: 394 [M^+], 376(35), 358(37), 348(40), 43(100); ^{1}H NMR(500MHz, C_5D_5N) δ: 0.97, 1.02, 1.35, 1.55, 1.64(each 3H,s,5×Me) 2.12(3H, s, OAc), 1.68(1H, dtd, J=13.1 3.5, 2.4Hz, H-1α), 1.75(1H, tdd, J=13.1, 3.5, 2.4Hz, H-1β), 1.67(1H, dtd, J=13.2, 3.6Hz, 2.6Hz, H-2α), 2.13(1H, tdd, J=13.2, 3.6, 2.6Hz, H-2β), 2.04(1H, dt, J=13.2, 3.6Hz, H-3α). 1.05(1H, td, J-13.2, 3.6, H-3β). 2.07(1H, d, J=2.2Hz, H-5α), 6.14(1H, dd, J=4.0, 2.2Hz, H-6α), 5.59(1H, d, J=4.0Hz, H-7α), 2.76(1h, d, J=18.2Hz, H-12α), 2.83(1H, d, J=18.2Hz, H-12β), 5.97(1H, dd, J=17.4, 10.8Hz, H-14), 4.41(1H, dd, J=5.4, 0.8Hz, H-15a), 4.97(1H, dd, J=10.8, 0.8Hz, H-15b). ^{13}C NMR(500MHz, C_5D_5N) δ: see Table 2.

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